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Letter to the Editor

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The invisible burden of multiple sclerosis: neuropsychiatric presentations and clinical pharmacology challenges

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Dear Editor,

Multiple sclerosis (MS) is a chronic central nervous system disease in which inflammation, demyelination, and neurodegeneration play interconnected roles. Thanks to significant advancements in disease-modifying therapies (DMTs) over the last two decades, relapse rates have been reduced and the progression of physical disability has been slowed.[1] Traditionally, MS has been evaluated primarily through its motor, sensory, and neuro-ophthalmological manifestations. However, a reality increasingly drawing attention is that neuropsychiatric presentations such as cognitive dysfunction, depression, and anxiety frequently emerge in early disease stages, sometimes even preceding physical symptoms.[2,3] In this context, I wish to highlight this often-overlooked neuropsychiatric burden and its associated clinical pharmacology challenges.

Neuropsychiatric symptoms including depression, anxiety, cognitive impairment, fatigue, sleep disturbances, and, rarely, psychosis are among the most significant yet underrecognized MS components.[2,3] In my clinical practice, I encountered a patient with MS who initially presented with acute psychosis, highlighting the profound impact of demyelination and neuroinflammation on cortical and limbic networks.[2] Cortical demyelination, gray matter atrophy, disruption of limbic connectivity, and chronic neuroinflammation are increasingly recognized as biological contributors to these psychiatric and cognitive manifestations rather than merely psychological reactions to chronic illness.[2,3]

Clinical management becomes highly complex at the intersection of neurological and psychiatric treatments. High-dose corticosteroids used in acute relapse treatment can cause significant psychiatric side effects such as insomnia, mania, and steroid-induced psychosis.[4] These manifestations can sometimes be confused with true disease activity. Similarly, interferon-beta's association with depression and the cardiac interaction risks of sphingosine-1-phosphate (S1P) receptor modulators with specific psychotropics demand careful monitoring.[4] Conversely, sedative psychotropics (e.g., benzodiazepines) can mimic MS progression by inducing cognitive slowing and balance impairment. For this reason, both neurologists and psychiatrists should exercise caution when prescribing medications to patients with MS.

From a clinical pharmacology perspective, the concomitant use of high-efficacy DMTs and psychotropic medications deserves particular attention.[4,5] In one of my patients receiving ocrelizumab (anti-CD20) therapy, leukopenia developed shortly after clobazam was initiated for psychiatric symptoms. Although a causal relationship cannot be established based on a single observation, this case underscores the importance of close hematological monitoring and multidisciplinary pharmacovigilance when psychotropic agents are introduced in patients receiving potent immunomodulatory therapies. It should not be forgotten that these observations are based on individual clinical cases and therefore should be interpreted with caution.

In conclusion, successful MS management is not limited solely to suppressing inflammation. Early recognition of psychiatric presentations and meticulous planning of psychopharmacological interventions are essential. A strong multidisciplinary collaboration among neurologists, psychiatrists, and pharmacologists will alleviate the mental burden of the disease and minimize pharmacological morbidity. To enhance quality of life and long-term treatment success, there is an urgent need for comprehensive clinical guidelines that address this intersection.

Sincerely,

ETHICAL DECLARATIONS

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This letter was externally peer-reviewed.

Conflict of Interest

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